A CEPSTRAL ANALYSIS OF EEG SIGNALS IN MOTION SICKNESS STUDIES

THESIS

Russel Brian Smith
Captain, USAF

AFIT/GSO/ENG/89D-1

DEPARTMENT OF THE AIR FORCE
AIR UNIVERSITY
AIR FORCE INSTITUTE OF TECHNOLOGY
Wright-Patterson Air Force Base, Ohio

AFIT/GSO/ENG/89D-1

A CEPSTRAL ANALYSIS OF EEG SIGNALS IN MOTION SICKNESS STUDIES

THESIS

Russel Brian Smith
Captain, USAF

AFIT/GSO/ENG/89D-1

Approved for public release; distribution unlimited.

AFIT/GSO/ENG/89D-1

A CEPSTRAL ANALYSIS OF EEG SIGNALS IN MOTION SICKNESS STUDIES

THESIS

Presented to the Faculty of the School of Engineering
of the Air Force Institute of Technology
Air University
In Partial Fulfillment of the
Requirements for the Degree of
Master of Science in Space Operations

Russel Brian Smith, B.S.
Captain, USAF

December, 1989

Preface

This research studied electroencephalographic (EEG) signals during the evolution of motion sickness. It used cepstral transformation techniques and hypothesis testing to investigate the relationships between phenytoin serum levels and malaise period EEG signals. It used the same techniques to study the relationships between phenytoin-malaise period EEG signals and placebo-malaise period EEG signals. It also studied the relationships between pre-malaise period EEG signals for phenytoin and placebo trials.

Many people helped me as I did this project. I want to thank my advisor, Dr. Kabrisky, for his encouragement and faith in what I was doing. I thank Dr. Chelen for sharing his vast knowledge and expertise in this field, and for keeping me from getting lost in all of it. I thank Lt. Col. Robinson for his patience in reviewing my work. I thank my GSO classmates for keeping me humble, and for helping me get through classes. And I thank those who have gone before for laying the foundation for this work.

I want to thank my wife, Kristi, for being my anchor in the midst of all the confusion, and for bearing with me through all of this.

And I thank God who makes everything possible.

Russ Smith

Table of Contents

List of Figures

List of Tables

Abstract

Eighteen male subjects were given the drug phenytoin in a double-blind, placebo-controlled crossover experiment. Subjects were rotated in a motion chair while eight physiological parameters were measured.

This research analyzed frontal-midline EEG signals for trends. Cepstral transformations were used to isolate peak-amplitude EEG frequencies during the evolution of motion sickness. Regression analysis and paired-t tests were applied to this data to identify relationships between phenytoin serum levels and EEG frequencies. Although the drug delayed or prevented the onset of emesis, no statistically significant relationships were found between phenytoin serum levels and frontal-midline EEG signals.

A CEPSTRAL ANALYSIS OF EEG SIGNALS IN MOTION SICKNESS STUDIES

I. INTRODUCTION

Background

Motion sickness is a generic term which encompasses air sickness, sea sickness, car sickness, space sickness, and any other form of sickness induced by perceived or actual motion. It is generally considered a disease, but is also a normal response to an abnormal environment (6:1). The four most common symptoms of motion sickness are nausea, vomiting, pallor, and cold sweating. Other associated symptoms are dizziness, disorientation, tingling in the limbs, fatigue, warmth, light-headedness, dry or acid mouth, stomachache, headache, anxiety, apathy, and in rare cases, unconsciousness (24:1).

The currently accepted explanation for motion sickness is the sensory conflict theory (SCT). The SCT is a theory which postulates that motion sickness occurs when the brain cannot reconcile various position and movement input data with established templates of similar inputs. This results in a condition that initiates the physiological state which can produce motion sickness (24:1-2). These input data come from the visual system, the semicircular canals, and the proprio-

ceptive sensors. The semicircular canals, located within the inner ear, are fluid-filled channels that detect motion and help control balance. Proprioceptive sensors permeate the muscles and joints of the body, and provide the brain with position and muscle tension data such as where the legs are in relation to each other (24:2). The templates are memories of a motion experience. The SCT asserts, that when during a motion event any two of the detection systems agree with each other, and the brain can correlate the event with a template, normal reactions to the event occur. However, if the detectors cannot agree, or if no template is present, one experiences the physiological upheaval commonly known as "motion sickness" (2).

Justification

Within the aerospace environment, motion sickness can be an extremely debilitating development that sometimes leads to fatal accidents. Dhenin reported that aircrew members often experienced motion sickness during maneuvering and aerobatics, during lengthy low altitude flights, and after simulator training (6:470-472).

Davis describes Space Motion Sickness as "the most clinically significant medical phenomenon during the first several days of spaceflight" (5:1185). He also reports that on the first 24 flights of the Space Shuttle, "The incidence of

[motion sickness] during a first Shuttle flight for 85 crewmembers was 67%" (5:1185). He then graded the specific occurrences using the criteria outlined in Figure 1.

SPACE MOTION SICKNESS
GRADING CRITERIA

None(0): No signs or symptoms reported with the exception of mild transient headache or mild decreased appetite.

Mild(1): One to several symptoms of a mild nature; may be transient and only brought on as the result of head movements; no operational impact; may include single episode of retching or vomiting; all symptoms resolved in 36-48 hours.

Moderate(2): Several symptoms of a relatively persistent nature which may wax and wane; loss of appetite; general malaise, lethargy and epigastric discomfort may be most dominant symptoms; includes no more than two episodes of vomiting; minimal operational impact; all symptoms resolved in 72 hours.

Severe(3): Several symptoms of a relatively persistent nature that may wax and wane; in addition to loss of appetite and stomach discomfort, malaise and/or lethargy are pronounced; strong desire not to move head; includes more than two episodes of vomiting; significant performance decrement may be apparent; symptoms may persist beyond 72 hours.

Figure 1: Space Motion Sickness Grading Criteria (5:1186)

Of the 57 cases (67% of 85), 26 (46% of 57) were rated "mild," 20 (35%) "moderate," and 11 (19%) "severe" (5:1186). The moderate and severe cases accounted for 54% of the reported cases of motion sickness.

Those crewmembers who experienced moderate or severe sickness were debilitated in some way so as to delay or degrade duty performance. In fact, Davis further reports that

"A Minimum Duration Flight (MDF) lasts at least three days in order to ensure that the crew has recovered for all entry and landing activities" (5:1185). Chelen related that on-orbit delays directly due to motion sickness cost NASA nearly $10 million per flight (2).

Consequently, motion sickness needs to be prevented or cured. Not only is it potentially fatal as in aircrew operations, but it is too expensive a problem to be left unsolved. Dr. Patricia Cowings, a NASA researcher states:

> Finding a solution to this biomedical problem has become a very high priority goal of the manned space-flight program because of its potential impact on crew safety, comfort and operational efficiency during Shuttle missions. (4:3)

Current Treatments

There are three major avenues of treatment for motion sickness: Desensitization, Autogenic-Feedback Training (AFT), and drug treatments.

Desensitization training is based on the theory that repeated exposure to stimulus eventually constructs a template wherein the brain will be able to resolve conflicting inputs. These templates will then prevent the onset of motion sickness. NASA's interest in this treatment stems from astronauts' reports of increased resistance to sickness-inducing stimulus after spaceflight (25:A1).

Problems exist with this form of training. It is expensive; those who are highly susceptible to motion sickness tend to adapt slowly, if at all. It is also extremely difficult to duplicate weightlessness in a 1-g environment for training purposes (4:2).

The objective of Autogenic-Feedback Training is to train crewmembers to prevent motion sickness. This is accomplished through Autogenic Therapy, which involves "physiological self-regulation" (4:3). One basis for using AFT is that during motion sickness, the body exhibits marked changes in many physiological parameters such as heart rate, breathing rate, and sweating. While it is currently questioned whether these changes are strictly effects or synergistic causes with the original stimulus, proponents of AFT contend that by controlling the physical manifestations of motion sickness, the skilled practitioner can control, or prevent, the onset of the illness (4:4).

AFT has shown only marginal results. Crewmembers trained in AFT demonstrated less than 60% increased resistance to sickness-inducing motion stimulus (4:52). Also, costs connected with AFT could reduce its even limited utility. First there is a time cost. Training times must be extended by as much as one year to include AFT (4:3). Second, not everyone can master the techniques of AFT (2). Finally, and not insignificantly, crewmember motivation may hinder learning (4:34).

Drug treatments, while holding much promise, have so far shown only limited success in mitigating motion sickness. Graybiel, et. al. have concentrated on testing four drugs in varying combinations:

1) Dramamine,

2) Scopolomine,

3) Promethazine, and

4) Dextro-amphetamine (Dexedrine)(12:773).

Graybiel tested volunteers in parabolic flight, administering 1, 2, and 3 by intramuscular injection. He reported that 62% of his subjects expressed some degree of relief from motion sickness (12:775). (However, his criteria for defining relief involved only the subject's ability to perform series of head motions, not the amelioration of the sickness.) The injections usually produced their effects within 10 minutes. Sickness was not prevented, but the symptoms were temporarily abated, and incapacitated subjects could resume their tasks (12:776). Davis reported that combinations of 2 and 4 were only marginally effective in treating space motion sickness (5:1188).

The principal obstacle in treating motion sickness with drugs is, as Harm states, "elucidating the specific physiological mechanisms and precise neural pathways responsible for the expression of motion sickness symptomatology" (13:7). In other words, researchers have yet to find the exact mechanisms

of cause and expression of motion sickness. Drugs influence specific cell sites and receptor functions. Without knowing those exact causes of motion sickness, drugs treatments will continue to show only marginal results.

Another major drawback of drug treatments is unwanted and possibly dangerous side-effects. All the drugs listed previously, except Dexedrine, are depressants (24:2). Dosage of the drug sufficient to prevent motion sickness has caused test subjects to become extremely disoriented and in some cases, induced stupor (2). Even in lower dosages that simply alleviate some of the symptoms, the drugs cause blurred vision, and drowsiness (12:775).

AFIT researchers, however, are currently experimenting with the drug phenytoin, commercially known as Dilantin. Dilantin has been successfully used for nearly 60 years to treat and prevent epileptic seizures. Chelen showed very low frequency brain waves which appeared during emesis as being similar to brain wave patterns sometimes associated with partial epileptic seizures (1:8). Tests performed on 16 subjects treated with Dilantin resulted in at least a 300% increased resistance to motion stimuli for 14 of those subjects. The other two suffered adverse reactions to the drug. The average increase was a factor of 6 to 8, and in some cases, Dilantin effected an equivalent cure (1:1). An added benefit of phenytoin is the absence of serious detrimental

side-effects when compared with other motion sickness prevention drugs.

Historical Indicators

ELECTROCARDIOGRAM (EKG):

The EKG measures the electrical potentials generated by the heart (24:5). AFIT researchers had used this primarily to monitor heart rates to detect possible occurrences of cardiac arrhythmias (24:5; 3). AFIT studies have reported a few instances of sinus arrest and bradycardia. Most notably, Hartle, McPherson, and Miller observed three separate cases (14:69). Only one case was reported in 1987, and this was detected during the recuperation period after the formal experiment (11:28). Since then, to avoid any danger to the test subject, AFIT researchers end experimentation upon first indications of serious arrhythmias (22:17).

ELECTRONYSTAGMOGRAPH (ENG):

The ENG measures the changes in potentials generated by movement of the choreo-retinal dipole of the eyes (24:6). Since 1985, AFIT researchers have used the traditional configuration of one set of ENG detectors to measure horizontal movements and another to measure vertical movements (22:18).

GASTRO-INTESTINAL MEASURES (GI):

Since 1986, AFIT researchers have measured GI abdominal surface potentials using techniques similar to traditional electrogastrography. A battery of paired electrodes was arrayed over the abdomen to detect and possibly localize sources of electrical activity. In 1987 the teams began using a phonosplanchnogram to record bowel sound activity (10:13). This device uses two very sensitive microphones to detect bowel sounds, and with a differential amplifier, cancels out common signals (presumably noise) leaving true bowel signals (2; 17).

PALLOR:

A photoplethysmograph (PPG) is used to optically measure relative blood flow at points on the skin surface (24:7). The 1985 and 1986 teams used both facial and finger PPGs. The 1987 team used only the facial PPG. The 1988 team used both facial and finger PPGs.

RESPIRATION:

AFIT researchers measured respiration with two different devices: a pneumograph to detect chest and abdominal expansion and contraction, and a spirometer to measure lung volume air flow during inspiration and exhalation (24:8). The

pneumographs are belts with implanted strain gauges which are wrapped around a subject's chest and/or abdomen.

All AFIT research teams used pneumographs to measure respiration. One was to measure only abdominal respiration, while the other measured only thoracic respiration (14:41). Additionally, they calibrated these gauges for each subject by comparing their data with actual breathing volumes derived from the spirometers (14:41).

ELECTROENCEPHALOGRAM (EEG):

EEG analysis in motion sickness has traditionally been confined to changes and abnormalities in the familiar range of brain wave activity. This range is delineated as follows: alpha waves--8 to 13 Hz; beta waves--14 to 30 or greater Hz; delta--1 to 3 Hz; theta--4 to 7 Hz (15:1) However, traditional analysis failed to find any significant EEG responses to motion sickness (3:3). It was not until after the 1986 AFIT team discovered a distinctive wave pattern below 1 Hz (the sub-delta range) that researchers investigated that region of the spectrum.

Chelen et. al. (in publication) first hypothesized that partial seizure activity was similar to motion maladaptation (3:8). That idea was tested by the 1988 AFIT team using Dr. Chelen's research protocol, "Evaluation of the Therapeutic Effects of Dilantin in Motion Sickness."

Problem Statement

The purpose of this thesis research was to continue collecting biophysical data on volunteer subjects, to analyze the data, and to improve upon motion sickness predictors developed by previous AFIT motion sickness research teams. As a corollary, it also studied the efficacy of the anticonvulsant drug phenytoin (Dilantin) on the evolution of motion sickness.

Scope

This research continued the AFIT motion sickness studies. It was limited to the following:

1. Collecting and analyzing EEG data on subjects up to 5 Sep 89. All 18 subjects included were male military personnel. Female subjects were not accepted in this effort since phenytoin is teratogenic and may affect potential pregnancies.
2. Analyzing the effect of phenytoin on motion sickness.
3. Improving on the mathematical models presently used to predict a test volunteer's subjective sense of motion sickness.

Assumptions

1. Motion sickness has a neurological basis. Specifically, it arises from sensory conflict.

2. Motion sickness is related to partial seizures.

3. Laboratory-induced motion sickness is similar to that observed in the real world.

4. The evolution of motion sickness produces distinct and measurable changes in physiological parameters.

5. The amount of change correlates to the level of motion sickness reported by the subject.

6. Motion sickness can be suppressed, precluded, or possibly cured with an anticonvulsant drug such as phenytoin.

7. Physiological parameters can be used to predict levels of motion sickness.

8. The observed physiological changes were in fact a result of motion sickness and not equipment malfunctions.

9. Subjects were accurate when reporting sickness levels.

Equipment and Materials

Equipment.

1. An electrically powered rotating chair, the associated control panel, and the following electrodes attached to each subject:

(a) A Marshall Electronics Astropulse 90 blood pressure cuff for measuring blood pressure;

(b) Two pneumographs for measuring abdominal and thoracic respiration;

(c) Three photoplethysmographs for measuring skin pallor;

(d) An INTECH Systems DIF-STET differential stethoscope (phonosplanchnograph) for recording audible gastrointestinal mechanical activity;

(e) Two electrosplanchnographs for electrical measurements of the gastrointestinal tract;

(f) Two electronystagmographs for measuring horizontal and vertical eye movement;

(g) An electrocardiograph for measuring heartbeat;

(h) Five electroencephalograph channels for measuring brain wave activity;

(i) A ballistocardiograph for measuring the force of the heart-beat.

2. The following recording instrumentation:

(a) A SOLTEC model 8K26 series 16-channel strip chart recorder;

(b) A Kyowa Dengo RTP-610 14-channel Beta tape recorder;

(c) A Zenith 248 personal computer for real-time data analysis.

3. Supplementary equipment included:

(a) A 16-channel low pass filter bank;

(b) A Spiropet hand-held spirometer;

(c) A Spirometrics, Inc., Flowmate Version 2.0 spirometer;

(d) A Cyborg Thermal P642 digital thermometer;

(e) A Realistic wireless FM microphone used to transmit subject's voice transmissions;

(f) An Ace bandage used in pallor calibration;

(g) A sphygmomanometer, also used in pallor calibration;

(h) A portable cassette tape player which played the recorded head movement commands;

(i) A Commodore 64 personal computer used to conduct cognition and performance tests before experiments;

(j) A Puritan-Bennet Corporation DATEX 223 Carbon Dioxide monitor.

Materials

1. The drug phenytoin;
2. Disposable Medtronic Medical "Huggables" infant monitoring electrodes used as electronystagmograph electrodes;
3. Disposable ConMed adult ECG electrodes used as electrocardiograph and electrosplanchnograph electrodes;
4. A standard issue Air Force flight sickness bag;
5. Alcohol pads used to clean subject's skin before electrode placement;
6. Platinum subdermal electrodes used as electroencephalograph electrodes;

7. Beta video tapes used in the 14-channel tape recorder;

8. Subject questionnaires and histories;

9. Analysis software:

   ASYSTANT, by Adaptable Laboratory Software, Macmillan Software Company;

   CODAS, by Dataq Instruments, Inc.;

   QUATTRO, by Borland; and

   STATISTIX, by NH Analytical Software.

Other Support

Dr. William Chelen (M.D., B.S.E.E.) was a important member of this research team. Having been continuously involved with the AFIT motion sickness research program since 1985, he provided critical corporate knowledge to this set of experiments. He devised and constructed most of the physiological sensors, including the very sensitive, extended-frequency-range electroencephalograph amplifiers. Dr. Chelen was responsible for screening and selecting potential subjects. He administered the anticonvulsant drug phenytoin. He conducted the pre-experiment physical exams. He monitored the well-being of the subjects during and after each experiment. Finally, he provided valuable direction for analysis.

II. PAST MOTION SICKNESS MODELS

This chapter discusses previous motion sickness models developed by AFIT research teams. One of the goals of AFIT research is to construct a reliable, consistent, and descriptive mathematical model to predict the evolution of motion sickness. Such a model would be useful in attempts to treat motion sickness through biofeedback or drug therapy. The following summary is not meant to denigrate the efforts of earlier teams, but to underscore the difficulties of collecting reliable and reportable data.

1983

Earl and Peterson, in 1983, began work to help the Neuropsychiatry Branch of the USAF School of Aerospace Medicine. They began to develop an automated data acquisition system to monitor "relevant physiological responses" in support of the School's autogenic-feedback training program (8:I-2). They assembled an integrated set of hardware that could measure, in real-time, the evolution of a subject's symptoms (8:I-4).

In line with autogenic-feedback training, they intended to measure the following parameters: pulse-to-pulse heart rate, gastric motility, respiration rate, and skin pallor (8:II-1). They published no data, but did recommend

> formulating a method of calculating a weighted sum of the relevant physiological measurements to

> determine a so-called 'motion sickness factor' (This quantity will show the advancement of motion sickness symptoms and may need to be adjusted for each individual being trained.) (8:I-2)

In essence, they recommended formulating a mathematical model to describe how the physiological measurements contributed to the evolution of motion sickness.

1984

In 1984, Fitzpatrick, Rogers, and Williams finished integrating the data collection computer and sensors started by Earl and Peterson. They were able to validate the concept of computerized data collection (9:6-1). They also published no data, but recommended experimental approaches and analysis techniques (9:6-2,3).

1985

The 1985 team of Jarvis and Uyeda took the first steps to develop a mathematical model. They noted percentage increases in skin pallor, galvanic skin resistance, and intestinal activity (16:105).

However, they had no standardized experimental protocol (16:76). This alone creates questions in their conclusions. Their sample size was very small, and the laboratory experienced constant air conditioning breakdowns (16:73, 92).

1986

In 1986, Hartle, McPherson, and Miller developed separate motion sickness equations. They each hypothesized a linear relationship between a subject's symptom level and the data collected from that subject (14:91; 18:47; 19:88). They then used multivariate statistics to construct equations relating a dependent variable, the reported symptom level, to a linear combination of independent variables, the biophysical data. The major criticism of these works is the arbitrary assumption of linearity between biophysical parameters and the evolution of motion sickness. Linear relationships between the data cannot explain the "avalanche phenomenon"--a slow build-up of motion sickness symptoms, followed by an extremely rapid onset of emesis. Miller himself reported this occurrence, but offered no explanation (19:67).

Since their data base consisted of only 12 subjects, the validity of the statistical results is questionable. Also, they did not use the same parameters for every subject (18:85-170).

Some of the team's data were also suspect. The laboratory was not air conditioned, yet some of the experiments took place in the summer when temperatures reached into the 80's. They collected data on surface skin temperature and galvanic skin response, which are greatly affected by sweating. Their findings could have been contaminated by the elevated room temperatures. Lastly, Drylie later reported that some sensor

application techniques irritated the skin, masking the physiological changes consequent to motion sickness (7:12).

1987

The 1987 team of Fix and Drylie continued the work of Hartle, McPherson, and Miller. Still faced with an uncontrolled environment, they installed a portable room air conditioner to attempt to maintain a workable temperature range. They also streamlined the subject preparation procedures, and refined methods to calibrate the sensors (7:10-11). They made a significant improvement in data accuracy by adding a filter bank to eliminate 60 Hz hum (7:13).

Fix modeled motion sickness with an equation and a neural network. Both used the same experimental data--electrosplanchnogram (ESG), electronystagmogram (ENG), thoracic respiration (THO), and galvanic skin resistance (GSR) (10:14).

Questions exist concerning the validity of the data. Even though the 1987 team took steps to control the experimental environment, they were still plagued with unreliable air conditioning equipment. Drylie noted that "it was sometimes possible to maintain the temperature in the ideal 22 to 24 degree Centigrade (71 to 75 degree Fahrenheit) range" (7:11). Both the ENG and GSR data can be greatly influenced by a subject sweating (2).

Since both of Fix's models depended on these data, it is not surprising that they were not accurate. Fix himself states

> One remaining problem: since this equation is an average of several subjects, it may not fit an individual subject. This problem is alleviated by using several parameters in the equation, but not completely. Therefore, there is a provision to multiply the output by a constant factor returned by the function fudge(). If the program consistently displays a number that is greatly different from the subject's reports, the operator types the number the subject is reporting. Fudge() then computes a factor that will move the indicator half the distance from the computed value toward the reported value (10:31-32).

Even with his "function fudge()", Fix's models reported sickness levels from 0 to 12, while actual subject reports ranged only from 0 to 10 (10:23). He was, however, the first AFIT researcher to report "recognizable patterns in the physiological data" (10:33). This laid the conceptual groundwork for the subsequent research teams to use more advanced neural networks in their analysis.

1988

The 1988 team of Scott and Morales modeled motion sickness using Abductive Reasoning Mechanism (ARM) software developed by Barron Associates (21). The ARM software is a neural net that relies on the concepts of abduction and polynomial network theory.

Abductive reasoning can be distinguished from both inductive and deductive reasoning. Abduction is "the act or process

of reasoning from a set of general principles to particulars or other general principles under uncertainty" (21:22). It is therefore similar to deduction. However, whereas deduction requires that a relationship exist between separate sets of data, abduction only needs a "consistency of the relationships among independent observations of the data" (21:22). Also, deduction uses the syllogism as its basic mechanism, while abductive reasoning uses abductive functions. An abductive function is "simply any function representing the relationships of a set of input variables to a set of outputs" (21:22).

The heart of ARM is the Algorithm for Synthesis of Polynomial Networks--ASPN. The objective of the ASPN process is to create a model as accurate as possible without overfitting the data (21:36). What sets ASPN apart from other modeling techniques is that few a priori assumptions about the model are required (21:35). Information is processed through a network from input variables to output variables. The network is called the abductive polynomial network (APN). Each node in the net represents a polynomial equation, and the connectivity coefficients are learned inductively (21:36). The ASPN then "finds the proper network structure and adjusts the coefficients within each node of the network to minimize either a predicted squared error or minimum description length modeling criterion" (21:36). Network modeling by polynomial

equations is based on Barron's interpretation of Kolmogorov's representation theorem. Montgomery cites Barron:

> four layer networks can represent any function provided elements are allowed which implement arbitrary continuous functions of one variable as well as elements which simply implement the sum of several variables (21:34).

Barron's foundational premise for ASPN, then, is that a network can model any function, provided it can implement continuous functions. The ARM software, therefore, works on the theory that

> if there exists a function that can model an underlying relationship among data, then that function can be represented by a network of arbitrary continuous functions, and since polynomials can approximate any continuous function, then polynomial networks can also model any function. Therefore, the problem can be reduced to one of discovering the polynomial network (as the abductive function) to model the relationships among variables given a data base of sample observations (21:34).

Essentially, if a functional relationship exists among the inputs, the ASPN can "discover" that function through interconnected polynomial equations. These equations then become the model of the particular inputs.

Scott modeled motion sickness using electrocardiogram (EKG), thoracic respiration (THO), electrosplanchnogram (ESG), facial photoplethysmograph (PPG), peripheral PPG, and nystagmus (ENG) parameters. He provides a detailed analysis procedure for eleven test subjects (24:34-39).

He calculated the heart rate for each subject while on placebo or phenytoin in each of the Graybiel sickness periods (20). He then found the arithmetic mean for each period, and measured the percentage increases from frank sickness to emesis in each trial. While on placebo, the average heart rate increased 10.8%. While on phenytoin, it increased 9.7% (24:39-40). These results agree in general with those reported by Gaudreault in 1987 (11:28). Scott concluded that average heart rates increased more while subjects were on placebo than while on phenytoin (24:39-40).

His analysis of thoracic respiration, ESG, and ENG data showed coinciding results: these parameters increased commensurately and almost equally on a percentage basis with the level of motion sickness. No significant statistical differences appeared (24:40,41,46). Drylie also noted similar results in 1987 (7:41-45).

Using data from subjects on phenytoin, his model predicted symptom levels within one number of reported levels 76% of the time. It estimated within two levels 95% of the time (24:50). However, with data from subjects on placebo, it was not as accurate. The ARM model values were within one level only 27% of the time, and within 2 reported levels 59% of the time (24:49).

Scott's data could be uncertain for two reasons. First, he too endured an unreliable air conditioning system. Again,

the ambient temperatures may have caused alteration of true nystagmus outputs by causing sweat artifacts. Second, he started with a small data base. He also extracted a larger data set for his placebo model than he had for his phenytoin model (24:86-87). He recognized that the differing data sets may partially account for the differences in accuracy of the two models (24:50).

Morales also applied the ARM software to create a motion sickness model. He furnished an outline of his analysis procedure (22:41-42). Additionally, he performed paired-t tests to analyze the means of the collected data for placebo and phenytoin trials.

He calculated mean heart rates for each subject while on placebo or phenytoin in each of the Graybiel sickness periods (20). His analysis showed that, for subjects on placebo, heart rates during frank sickness were 26% greater than heart rates during the pre-experiment control period. Also, the mean heart rates did not recover to baseline levels until five minutes after emesis (22:43).

For those subjects on phenytoin his analysis showed that, in general, heart rates decreased with the evolution of motion sickness. An increase in mean heart rate did occur during the baseline period, but Morales attributes this to pre-experiment anxiety. Mean heart rates dropped to baseline levels within one minute after emesis (22:43).

His paired-t test suggested that mean heart rates for subjects on phenytoin were lower than heart rates of those on placebo. This conclusion agrees with Scott and Gaudreault.

Morales' conclusion concerning thoracic respiration was similar to Scott's: mean respiration volumes increased about equally during the evolution of motion sickness for both placebo and phenytoin trials. He found no significant differences in respiration volumes (22:50). He did find, though, that recovery times to baseline levels were very different. With phenytoin, respiration volumes returned to normal three minutes after emesis. However, for those on placebo, respiration volumes were not to baseline levels even five minutes after emesis (22:47).

Morales found no significant differences in ESG data for those on placebo versus those on phenytoin. He did find that maximum levels were reached in different sickness periods, but offered no conclusions (22:50).

Morales examined delta-range EEG data by looking first at root-mean-square (rms) voltages, then at peak voltage levels. In the rms analysis, for the placebo trials, he found that the maximum rms voltages were during Graybiel period MIIA. He also stated that EEG rms voltages never reached baseline levels as long as five minutes after emesis (22:54).

For the dilantin trials, all subjects had higher EEG rms voltages during control periods before the experiments than

during the same control periods of the placebo trials. Subjects on phenytoin also showed lower post-emesis rms voltages than control period rms voltages. Morales states "This [sic] data suggest that dilantin [phenytoin] may be increasing the EEG subdelta-delta voltages". He concludes, however, that "the EEG RMS voltages for subjects...treated with the placebo are not significantly different from EEG RMS voltages for subjects...treated with dilantin [phenytoin]" (22:54). (Author's note: Subdelta-delta refers to EEG frequencies below the nominal delta range frequencies of 1-3 Hertz.)

In his analysis of peak voltages, Morales showed almost identical results. He again suggests that dilantin [phenytoin] may be increasing EEG subdelta-delta voltages. He also concludes that "the data suggest that the EEG peak voltages for subjects ...treated with the placebo are not significantly different from EEG peak voltages for subjects...treated with dilantin (22:58).

As stated earlier, Morales used his results in the ARM software to create a model of motion sickness. He first used each individual parameter in both the placebo and phenytoin trial--heart rate (from EKG), thoracic respiration volume (THO), electrosplanchnogram (ESG), and electroencephalogram (EEG)--to build a model. As could be expected, no parameter by itself constructed a reliable model. Each had, in an output range of 1 - 16, a standard deviation over 4 (22:71-85).

He then used all four parameters together to construct a model. For the placebo trials, the ARM software discarded the eeg parameter entirely in the equation formulation (22:90). This model proved to be only slightly more accurate than the individual models, having a standard deviation from the true output of 4.088 (22:90).

The model for the phenytoin trial parameters also discarded the eeg data. This model proved to be the most accurate with a standard deviation of 3.89 (22:92). Morales offers no discussion concerning these different results.

III. EXPERIMENTAL PROCEDURE

The research described here used a double-blind, placebo controlled crossover technique to investigate the effectiveness of phenytoin in the treatment of motion sickness. Specifically, it investigated the impact phenytoin serum levels have on frontal-midline EEG frequencies. This chapter includes information on the equipment used in the experiment, the screening of potential subjects for the experiment, and the experimental procedure.

Equipment

A complete list of equipment use can be found in Chapter I, EQUIPMENT AND MATERIALS section.

Movement of the rotating chair coupled with directed head movements produced suitable coriolis stimulation to bring on symptoms of motion sickness. The Realistic FM microphone, the Marshall sphygmomanometer, and the physiological amplifiers were mounted to the rotating chair. Data from the amplifiers went through slip-rings within the chair to the 16-channel low pass filter bank. These data were then routed to the strip chart recorder, the Beta tape recorder, and the Z-248 microcomputer (AT class). For a detailed description of the amplifiers, see Gaudreault (11:21-24). Figure 2 shows the

placement of the silver/silver chloride electrodes, strain gauges, photoplethysmographs, and differential stethoscope.

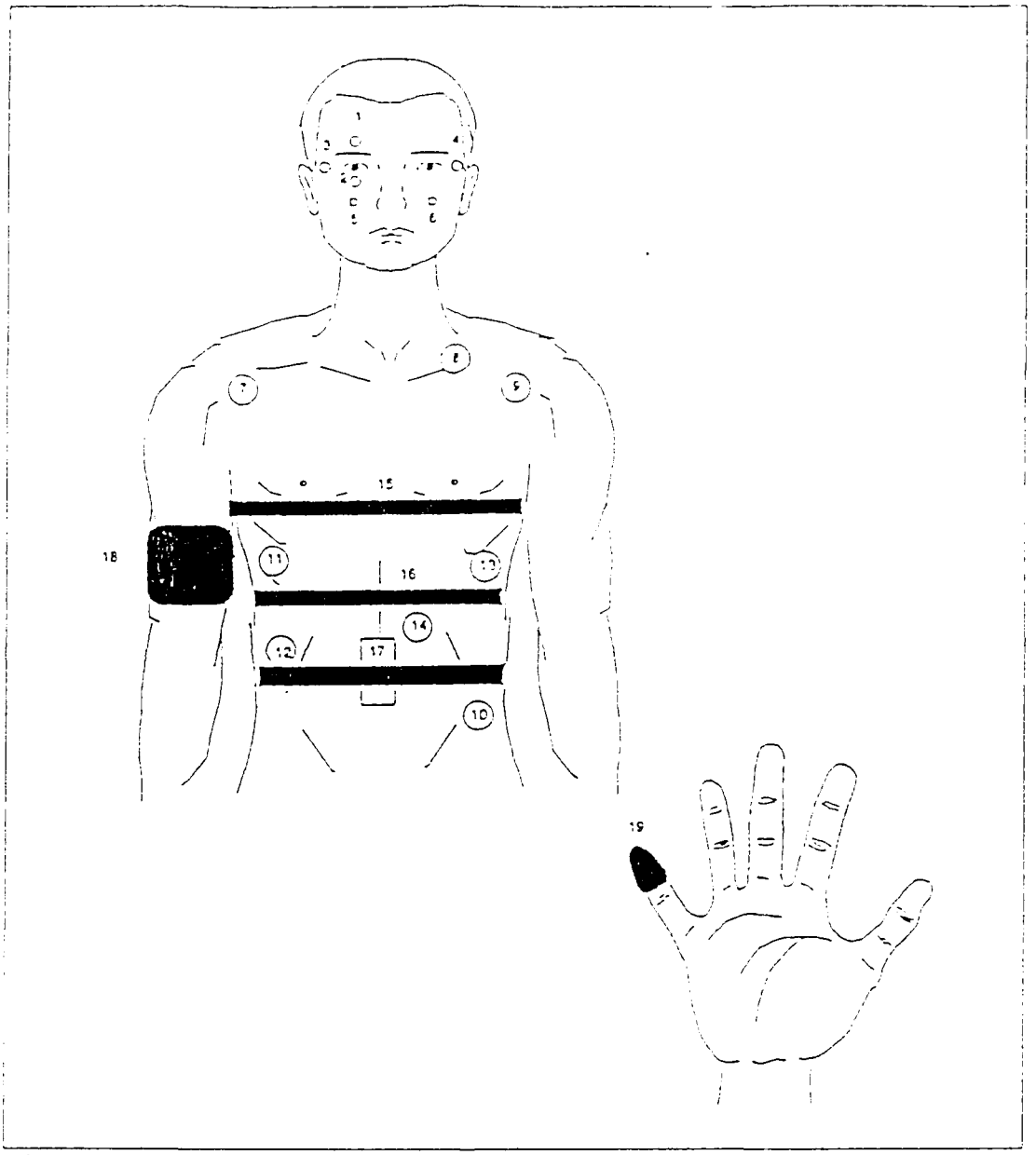

Figure 2: Body Sensor Placement (22:34)

The numbers 1-19 refer to sensor-pair identifiers. Sensors 8 and 9 are electrical grounds. Sensor 18 is the Marshall sphygmomanometer cuff.

Nystagmus data were collected using two pairs of Huggables electrodes. One set placed above and below an eye measured vertical nystagmus. The other, placed on each temple, measured horizontal movement. See Figure 2, numbers 1-4.

Pallor data were collected with two facial photoplethysmographs and one finger photoplethysmograph. The finger sensor also measured blood pulse volume. See Figure 2, numbers 5,6, and 19. Pallor sensors were calibrated on the subject's hand. The hand was exsanguinated by wrapping with the Ace bandage and using a sphygmomanometer. This blood-free state determined maximum pallor. After several minutes, the sphygmomanometer was released, allowing calibration at maximum flush.

Electrocardiograph data were collected through a lead II configuration using the ConMed electrodes (22:32). See Figure 2, numbers 7 and 10.

Gastrointestinal (GI) activity was measured using two different types of sensors. Electrosplanchnographs measured GI electrical activity. The DIF-STET differential stethoscope measured bowel sounds. See Figure 2, numbers 11-14, and 17.

Respiration data were collected using two strain gauge belts and the Puritan-Bennet Carbon Dioxide Monitor. One belt

was attached around the chest and detected thoracic respiration, while the other was attached around the mid-section and detected diaphragmatic respiration. See Figure 2, numbers 15 and 16. Each subject inserted the carbon dioxide detector into his right nostril and secured it with medical adhesive tape. The detector is a small, plastic cone open at both ends, and connected to the Monitor with a thin, flexible hose.

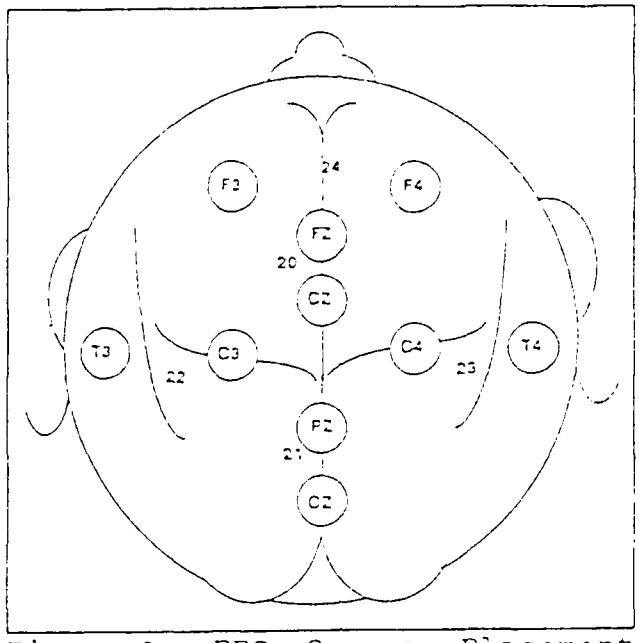

Figure 3: EEG Sensor Placement (22:35)

Figure 3 shows the placement of platinum subdermal electrodes on the scalp (22:34-35). Electroencephalographic data were collected using ten subdermal electrodes. They were configured using a bipolar channel arrangement consisting of the Fz-Cz channel, the Pz-Oz channel, the C4-T4 channel, the T3-C3 channel, and the F3-F4 channel (22:33).

Screening

The screening phase was intended to eliminate any potential subject with abnormal vestibular functions, or whose

health could have been at risk as a result of this experiment. It consisted of a medical history and motion sickness history interview, balance tests, a motion susceptibility trial, a physical examination, blood tests, and performance-cognition tests.

Each potential subject completed a questionnaire about their medical and motion sickness history. Individuals with familial or genetic disorders, or chronic or systemic diseases were excluded. Subjects rated themselves on how susceptible they were to motion sickness, and which types of motion were most provocative to them.

Subjects performed tandem Romberg and one-legged balance tests to determine if they had a normal vestibular system. This procedure eliminated visual inputs and forced the subjects to rely on the proprioceptive and vestibular systems to maintain balance. Those who consistently lost their balance were eliminated from the research because it was felt they would not be susceptible to coriolis induced stimulation.

The susceptibility trial helped determine the subject's sensitivity to motion stimuli. Each subject rode in the rotating chair at speeds from 12 to 22 rpm (determined from susceptibility inquiries on the medical questionnaires) for several minutes. Noninstrumented, blindfolded subjects rode in the chair and performed directed head motions. They were closely monitored and frequently asked to report their

symptoms. The subjects themselves controlled the duration of this phase. They were instructed to continue only until they felt moderate nausea. When they began to feel sick, they were to signal and the run would then end.

A complete physical examination was performed on each subject. Only those individuals in good health continued in the experiment.

Each subject then went to the base hospital for more testing. They underwent a complete blood count, lipid and cholesterol counts, urinalysis tests, liver function tests, and a general battery of blood biochemistry tests (Chem 18).

After the physical examinations, the subjects then had their cognitive and physical performance abilities tested. Personal-computer based tests developed by the Air Force Aerospace Medical Research Laboratory provided baseline data on reasoning ability, visual acuity, and manual response speed and accuracy. These data were compared with pre-trial tests to determine if any performance effects resulted from the phenytoin.

Procedure

After successful screening, Dr. Chelen administered a test dose of phenytoin to each subject. He then carefully monitored the individual for their reaction to the drug. If no adverse result ensued, the subject was allowed to leave.

Dr. Chelen would check again that evening. He would make a final check the next day. If at any point unfavorable symptoms appeared, the subject would not be allowed to continue in the experiment.

Each subject's trial began the day before their rotating chair ride. They were given two envelopes, A and B, containing five capsules of a dextrose placebo or phenytoin. Only the principal investigator, Dr. Chelen, knew which envelope contained which substance. The subject would choose an envelope from which to take capsule for the first trial. The remaining envelope would be used for the second trial (at least one week later). Only after the second trial would the subject reveal the order of the capsules he took. The subject would take the first capsule in the late afternoon. The remaining four were scheduled as follows: one with that evening's dinner, one with food before bed, one with breakfast the next morning, and one with lunch. The trial would then start in the early afternoon.

About one hour before the experiment, each subject executed the performance-cognition test battery. Dr. Chelen would then interview the subject about their reactions, if any, to the capsule they took. Dr. Chelen would conduct a brief physical examination which included an eye test for acuity, range-of-motion, and nystagmus.

Once these preliminaries were complete, the research team began to outfit the subject with the physiological monitoring devices and sensors. Pallor sensors were calibrated. Blood would be drawn to measure phenytoin serum levels. After all electrodes and belts had been attached, the subject was helped into the motion chair. Respiration calibration was done. The subject would be blindfolded and nystagmus calibration finished.

At this point, chair velocity needed to be calculated. The desired length of the experiment was approximately 15 minutes. This would enable the team to gather sufficient data and minimize subject discomfort. The AFIT protocol prescribed head motions every ten seconds, so 15 minutes allowed for 90. According to Miller and Graybiel, chair speed is related to an individual's Coriolis Sickness Susceptibility Index, or CSSI. The CSSI is the product of the Graybiel "E-factor" and N, the number of head motions needed to elicit MIII:

$$CSSI = E \times N \qquad (20:10) \qquad (1)$$

Miller and Graybiel also determined that for their subjects, the CSSI, while ranging from 0.4 to 100, had a mean of 15.3 (20:11). Using this mean value, and fixing N to be 90, a value for E can be easily determined. Once E is found, an appropriate chair velocity can be found from Figure 4. In this case, E equals .167, and the chair speed is approximately 15 rpm. Each subject's chair velocity was adjusted according to

personal motion sickness history and results from the susceptibility run.

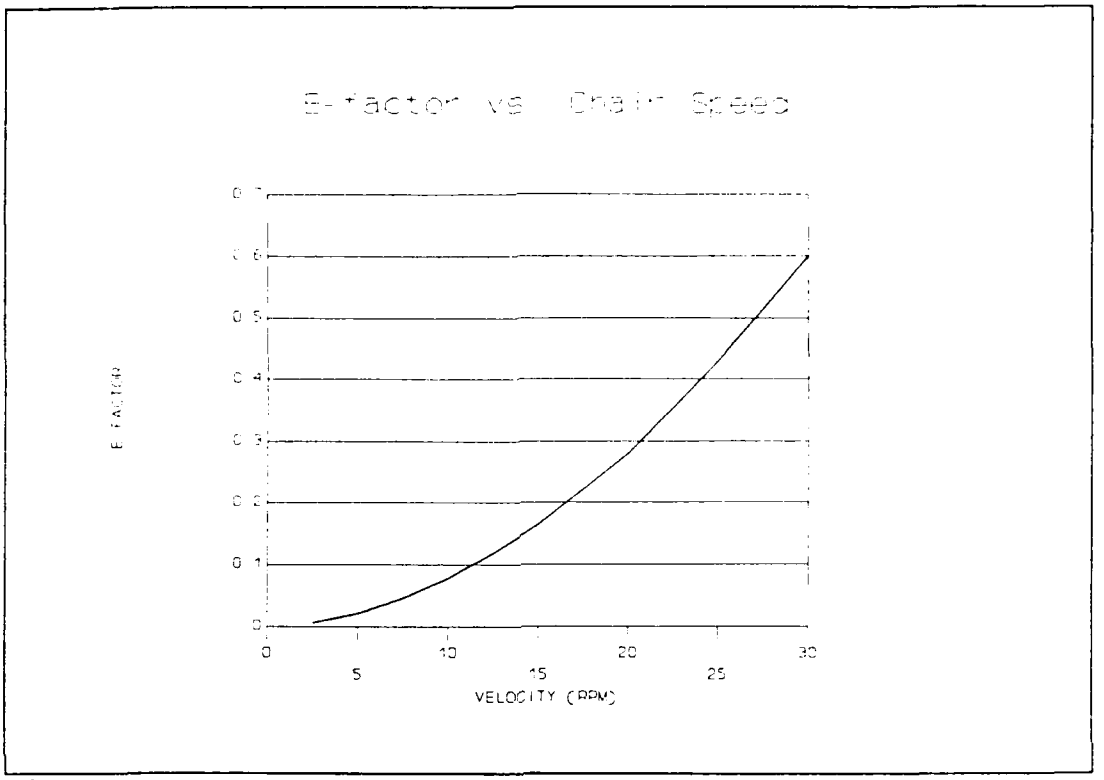

Figure 4: E-factor vs. Chair Speed (20:10)

The subject rested for about five minutes to gather baseline data. The chair would then be slowly accelerated to the predetermined rotation speed. An audio tape directed head movements. The team constantly monitored the individual. He was regularly asked about his symptoms and to rate them on a scale of 1 (normal) to 10 (imminent emesis). The experiment continued until emesis or until the subject elected to terminate the experiment.

At the end of the experiment, the chair was slowly decelerated and stopped. The subject remained seated to allow

recovery and to collect ten minutes of post-emesis data. The subject was then helped out of the chair, cleaned up, and released.

IV. RESULTS FROM THE 1989 DATA

Data Collection Method

Data were collected on subjects completing the procedure detailed in Chapter 3. The physiological signals from the EEG sensors were routed through 80 dB amplifiers to slip-rings in the rotating chair, and then into a sixteen channel low-pass filter. This filter provided a 12 dB per octave rolloff above 30 hertz (2). A Kyowa-Dengo RTP-610A data recorder captured the data on 14-channel beta tape. Data were simultaneously recorded on a SOLTEC model 8K26 strip chart.

Data Analysis Method

Electroencephalogram (EEG) data from the frontal midline region of 18 male subjects were analyzed. Additionally, the Miller and Graybiel diagnostic scale was employed to quantify subjects' malaise periods during motion sickness (20). Data were collected for both placebo and phenytoin trials. The data analysis procedure is outlined below:

I. Review and analyze strip charts.

A. Determine beginning and end points of the baseline period (BL)-- fully instrumented subject in chair, before rotation.

B. Determine beginning and end points of the symptomatic periods as defined by Graybiel. These are MI, MIIB, MIIA, MIII, and Frank Sickness (FS). In this study, Frank Sickness is the period during, and immediately after, emesis.

II. Associate the corresponding beta-tape counter numbers with the periods found in step I.

III. Analyze beta tapes. EEG data were digitized at 100 samples per second using CODAS software into files at least 22 seconds long. Motion artifacts were manually edited out during this step.

IV. Perform cepstral transformations. Sample files of 2048 data points were processed into cepstral form and analyzed using ASYSTANT software. See Appendix C for discussion of cepstral analysis. The peak-amplitude quefrency per file and its corresponding frequency were also determined using ASYSTANT. Appendix A shows these amplitudes and frequencies.

V. Perform statistical analysis. Regression analysis and hypothesis tests were accomplished to

discover if the effect of phenytoin was statistically discernible on frontal-midline EEG frequencies. Appendix B tabulates the means and standard deviations for each subjects' EEG frequencies for symptomatic periods.

Results

The following data sets were analyzed: 1) Phenytoin serum level (LEV) versus Mean symptomatic EEG frequency for phenytoin trials (FREQP), 2) Phenytoin serum level versus Baseline EEG frequency for phenytoin trials (BLP), 3) Phenytoin serum level versus the Number of symptomatic periods per phenytoin trial with subdelta EEG frequencies (NUMP) (Subdelta EEG frequencies are those frequencies below the nominal range of 1 - 3 Hz), 4) Mean symptomatic EEG frequency for phenytoin trials versus Mean symptomatic EEG frequency for placebo trials (FREQPL), 5) Baseline EEG frequency for phenytoin trials versus Baseline EEG frequency for placebo trials (BLPL), and 6) Number of symptomatic periods per phenytoin trial with subdelta EEG frequencies versus the Number of symptomatic periods per placebo trial with subdelta EEG frequencies (NUMPL).

Hypothesis testing techniques and regression analysis were used to compare the phenytoin trial data against the phenytoin

serum level per subject and the placebo trial data. The Wilk-Shapiro test for normality was accomplished (Table I).

Table I. Results of Normality test

Normality Coefficients

Variable	Wilk-Shapiro Number
FEV	.8710
FREQP	.9815
FREQPL	.9629
BLP	.7208
BLPL	.8947
NUMP	.8569
NUMPL	.9306

The range of values for the Wilk-Shapiro number is 0 - 1. A value of 1 indicates perfectly normal data. If conditions for normality were sufficient, two-tailed paired-t tests were used. If the data was not shown to be normal, the Wilcoxon Signed Rank Test was used. The null hypothesis assumed that phenytoin serum levels produced no significant impact on frontal-midline EEG frequencies. The alternate hypothesis assumed that it did have a discernible impact. Significance levels are indicated. All p-values listed are one-tail values.

1. Phenytoin serum level versus Mean symptomatic EEG frequency for phenytoin trials:

The phenytoin serum level per subject compared with that subject's mean EEG frequency (Table II) is depicted in Figure 5. No trend is readily observable. Regression analysis suggests no relationship between phenytoin levels and mean EEG frequency (significance level = .05, t-statistic = 1.45, p-value = .0836, r-squared = .1158).

Table II. Phenytoin serum level and Mean symptomatic period EEG frequencies

Phenytoin level vs. mean frequency per subject

blood level	sub no.	mean freq
10.1	7	2.91
10.4	4	4.74
11.4	16	2.81
11.7	3	2.49
12.0	9	0.75
12.0	12	0.26
12.3	2	0.29
12.3	8	2.13
12.4	1	4.88
13.0	10	2.64
14.0	14	3.57
14.7	13	1.19
15.1	15	3.98
16.2	18	2.05
17.3	11	1.40
18.2	5	6.30
18.5	6	5.35
23.9	17	3.94

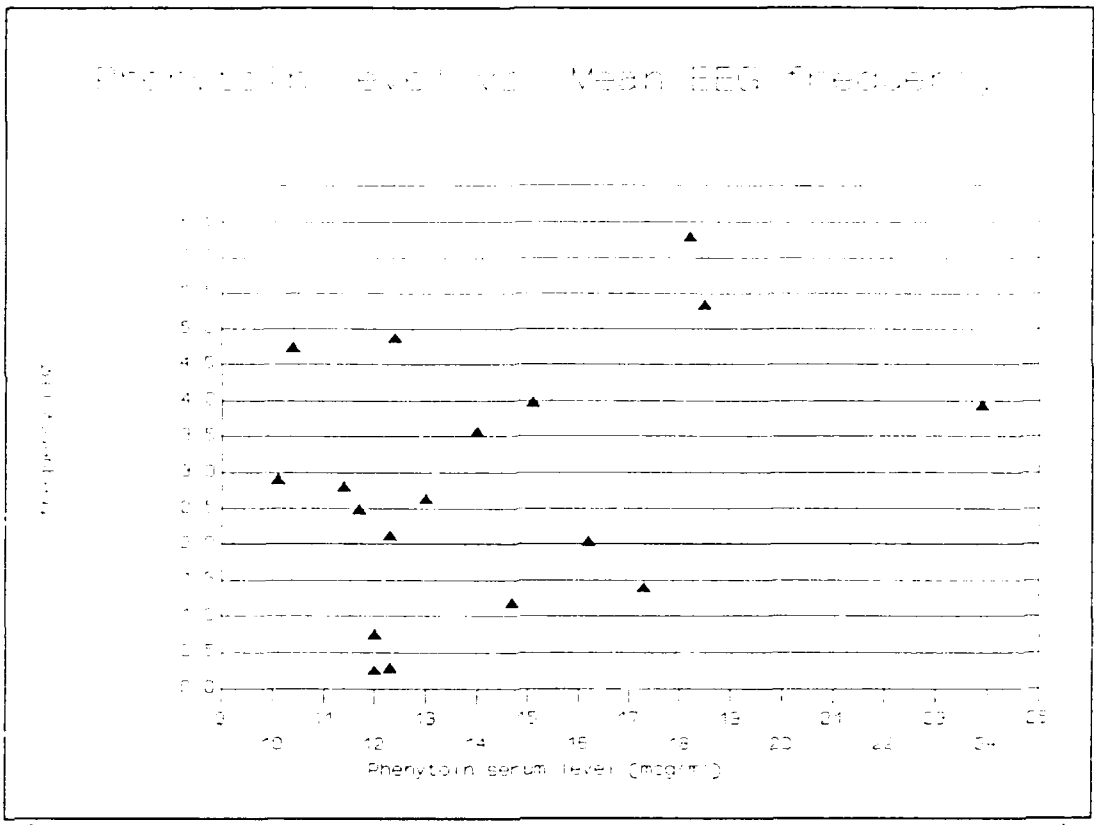

Figure 5. Phenytoin serum level versus Mean symptomatic period EEG frequency

Figure 5 graphically represents Table II. Mean symptomatic period EEG frequency is the mean EEG frequency of malaise periods MI through FS during each subject's phenytoin trial. Abscissa is indexed by increasing phenytoin level per subject.

2. Phenytoin serum level versus Baseline EEG frequency for phenytoin trials:

The phenytoin serum level per subject compared with that subject's Baseline EEG frequency (Table III) is depicted in Figure 6. No trend is readily observable. Regression analysis suggests no relationship between phenytoin levels and baseline EEG frequency (significance level = .05, t-statistic = .58, p-value = .2843, r-squared = .0207).

Table III. Phenytoin serum level and Baseline frequency while on phenytoin

Phenytoin level vs. Phenytoin Baseline frequency (Hz)

phenytoin level	subject number	BL freq phenytoin
10.1	7	0.10
10.4	4	0.138
11.4	16	0.90
11.7	3	3.94
12.0	9	0.105
12.0	12	5.39
12.3	2	0.276
12.3	8	0.115
12.4	1	0.276
13.0	10	1.83
14.0	14	0.127
14.7	13	6.024
15.1	15	0.12
16.2	18	0.224
17.3	11	6.4
18.2	5	0.488
18.5	6	4.88
23.9	17	0.276

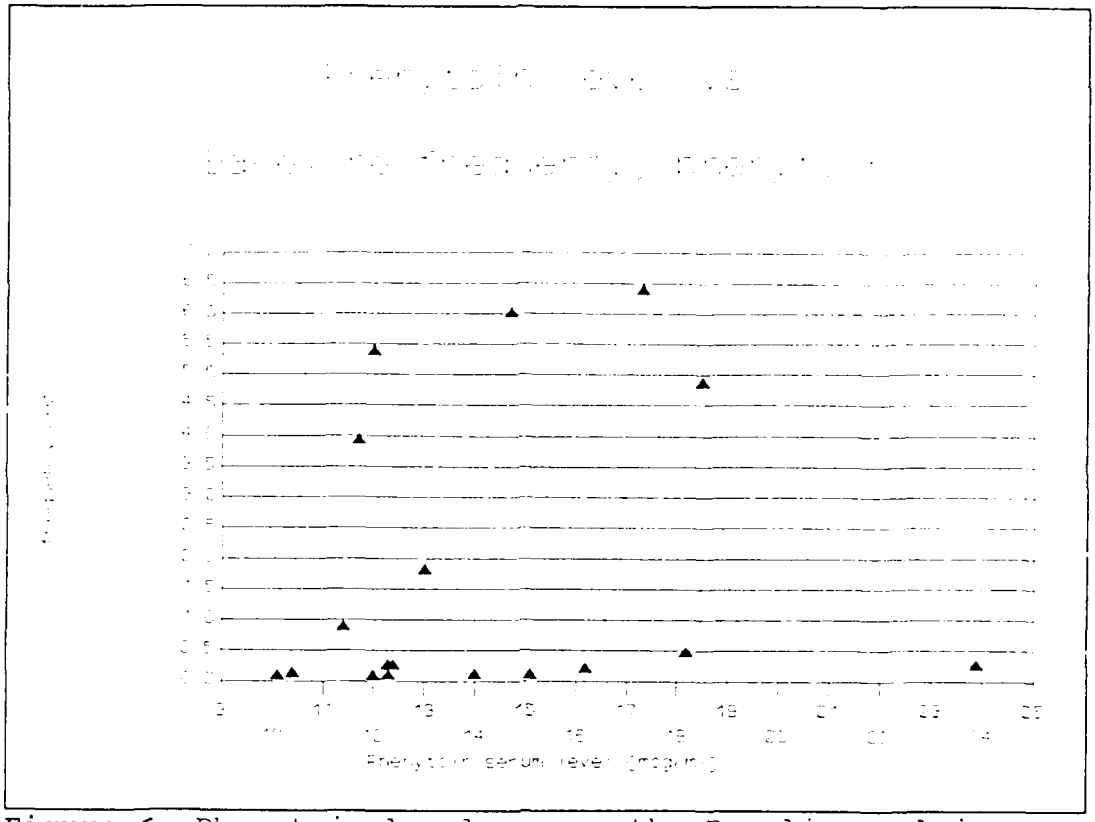

Figure 6. Phenytoin level versus the Baseline malaise period EEG frequency

Figure 6 graphically represents Table III. Baseline frequency is the frequency during the Baseline period (subject in chair, before rotation) EEG frequency during each subject's phenytoin trial. Abscissa is indexed by increasing phenytoin level per subject.

3. Phenytoin serum level versus the Number of symptomatic periods per phenytoin trial with subdelta EEG frequencies:

The phenytoin serum level per subject compared with the number of malaise periods with subdelta frequencies as the peak-amplitude frequency for each subject's phenytoin trial (Table IV) is depicted in Figure 7. A trend is not readily observable. Regression analysis suggests no relationship between phenytoin levels and the number of periods with subdelta frequencies (significance level = .05, t-statistic = 1.22, p-value = .1197, r-squared = .0854).

Table IV. Phenytoin serum level and the Number of periods with subdelta frequencies while on phenytoin

Phenytoin serum level vs. Number of periods with subdelta frequencies while on phenytoin

phenytoin level	subject number	number of periods
10.1	7	2
10.4	4	1
11.4	16	1
11.7	3	2
12.0	9	4
12.0	12	3
12.3	2	1
12.3	8	0
12.4	1	0
13.0	10	1
14.0	14	0
14.7	13	4
15.1	15	1
16.2	18	1
17.3	11	3
18.2	5	0
18.5	6	0
23.9	17	0

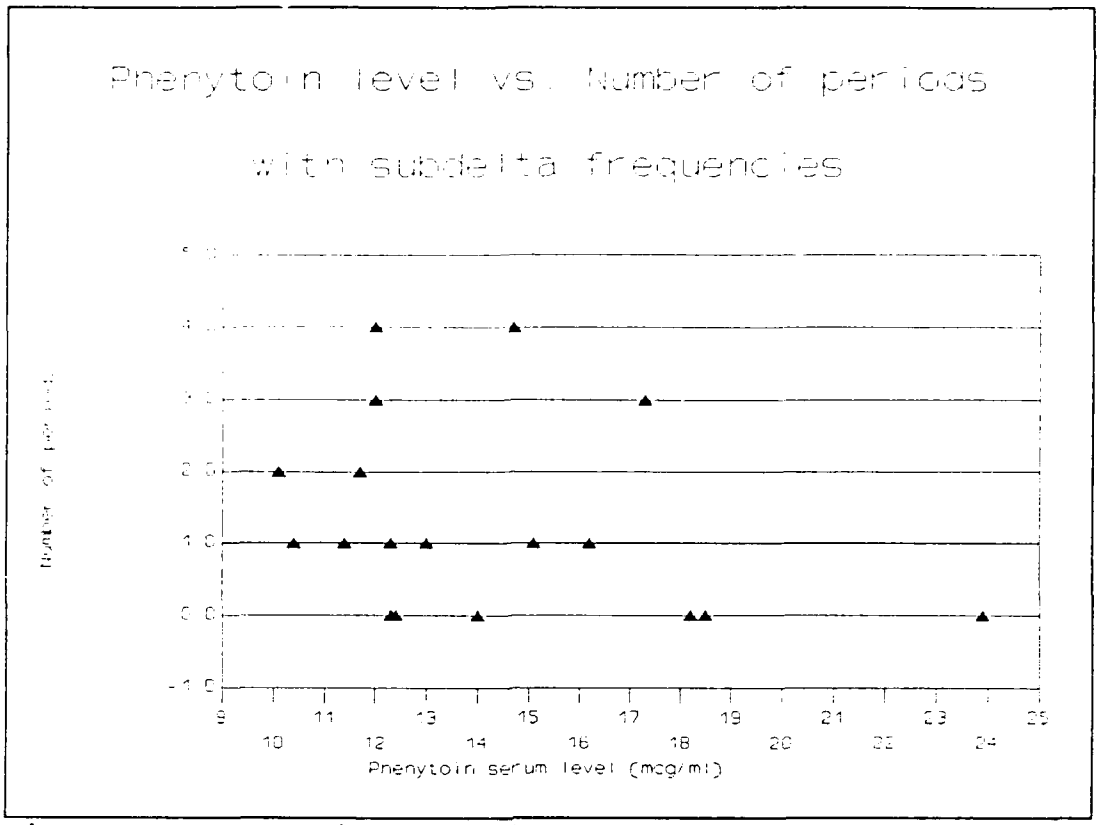

Figure 7. Phenytoin serum level versus the Number of malaise periods with subdelta frequencies while on phenytoin

Figure 7 graphically represents Table IV. Abscissa is indexed by increasing phenytoin level per subject. Number of periods is the number of periods during the phenytoin trial that each subject had a subdelta (< 1 Hz) EEG frequency as the peak-amplitude EEG frequency. For instance, subject 13 reported symptoms in all malaise periods MI through FS. Of those five periods, 4 contained a subdelta frequency as the peak-amplitude frequency.

4. Mean symptomatic EEG frequency for phenytoin trials versus Mean symptomatic EEG frequency for placebo trials:

The mean EEG frequency for subjects during symptomatic malaise periods while on phenytoin compared with the mean EEG frequency during symptomatic malaise periods while those subjects were on placebo (Table V) is depicted in Figure 8. No trend seems to be readily observable, but the Wilcoxon test calculated a p-value of .0886. At a .05 significance level, this suggests that phenytoin levels have no impact on mean symptomatic period EEG frequencies.

Table V. Mean symptomatic EEG frequency, phenytoin and Mean symptomatic EEG frequency, placebo

Phenytoin Mean FEG frequency vs. Placebo Mean EEG frequency (Hz)

mean frequency phenytoin	subject number	mean frequency placebo
2.91	7	0.54
4.74	4	3.27
2.81	16	2.77
2.49	3	2.00
0.75	9	1.07
0.26	12	3.10
0.29	2	3.23
2.13	8	0.57
4.88	1	2.36
2.64	10	2.68
3.57	14	1.62
1.19	13	2.84
3.98	15	1.19
2.05	18	0.16
1.40	11	1.45
6.30	5	1.40
5.35	6	3.79
3.94	17	2.83

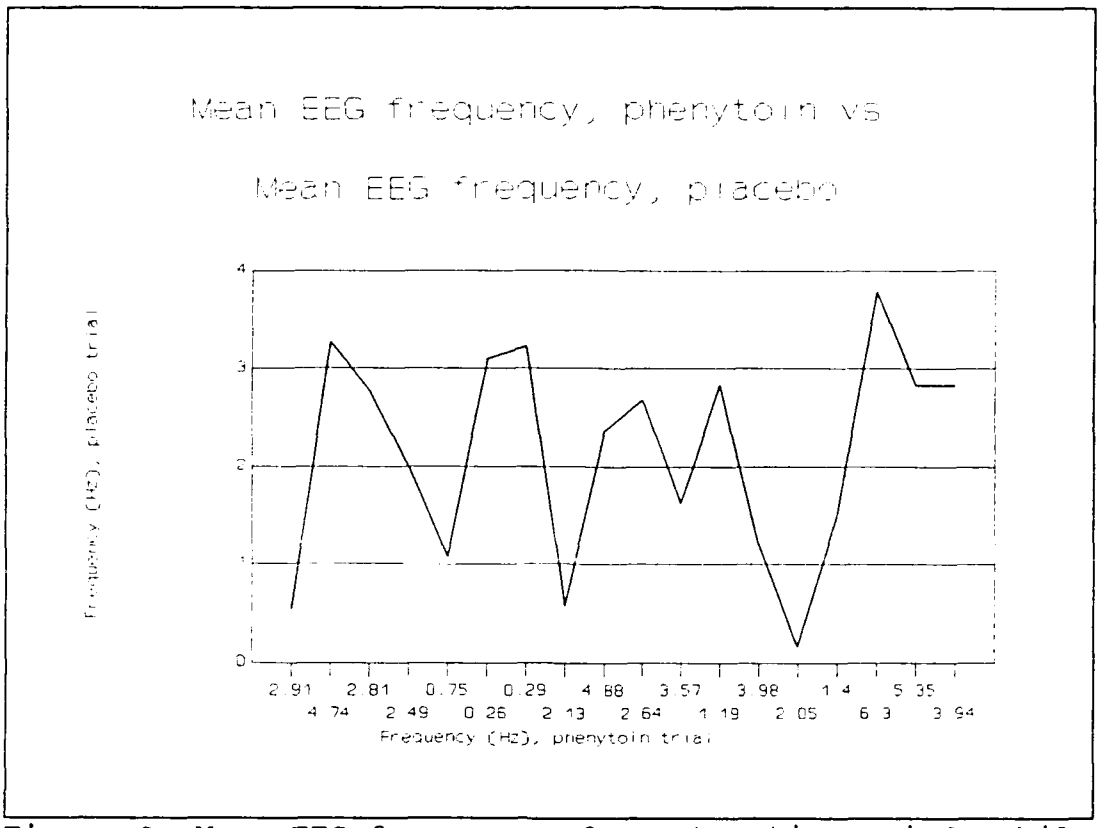

Figure 8. Mean EEG frequency of symptomatic periods while on phenytoin versus Mean EEG frequency of symptomatic p-eriods while on placebo

Figure 8 graphically represents Table V. Mean EEG frequency is the mean EEG frequency of malaise periods MI through FS during each subject's phenytoin or placebo trial. Abscissa is indexed by mean EEG frequency per subject, and ordered by increasing phenytoin level per subject.

5. Baseline EEG frequency for phenytoin trials versus Baseline EEG frequency for placebo trials:

The Baseline period EEG frequency for subjects while on phenytoin compared with the Baseline period EEG frequency for those subjects while on placebo (Table VI) is depicted in Figure 9. It appears graphically that some similarity exists between these two data sets, but the Wilcoxon test calculated a p-value of .0231. At a significance level of .05, this implies that phenytoin may have an impact on baseline EEG frequencies.

Table VI. Baseline EEG frequencies while on phenytoin and Baseline EEG frequencies while on placebo

Phenytoin Baseline frequencies vs. Placebo Baseline frequencies (Hz)

subject number	BL freq phenytoin	BL freq placebo
7	0.100	0.276
4	0.138	6.830
16	0.900	0.794
3	3.940	11.380
9	0.105	5.120
12	5.390	5.680
2	0.276	*
8	0.115	1.310
1	0.276	4.880
10	1.830	0.742
14	0.127	0.416
13	6.024	5.390
15	0.120	0.179
18	0.224	0.205
11	6.400	6.400
5	0.488	3.530
6	4.880	3.200
17	0.276	6.400

(*) Due to an equipment malfunction, no data were recorded for Subject 2 during his baseline period.

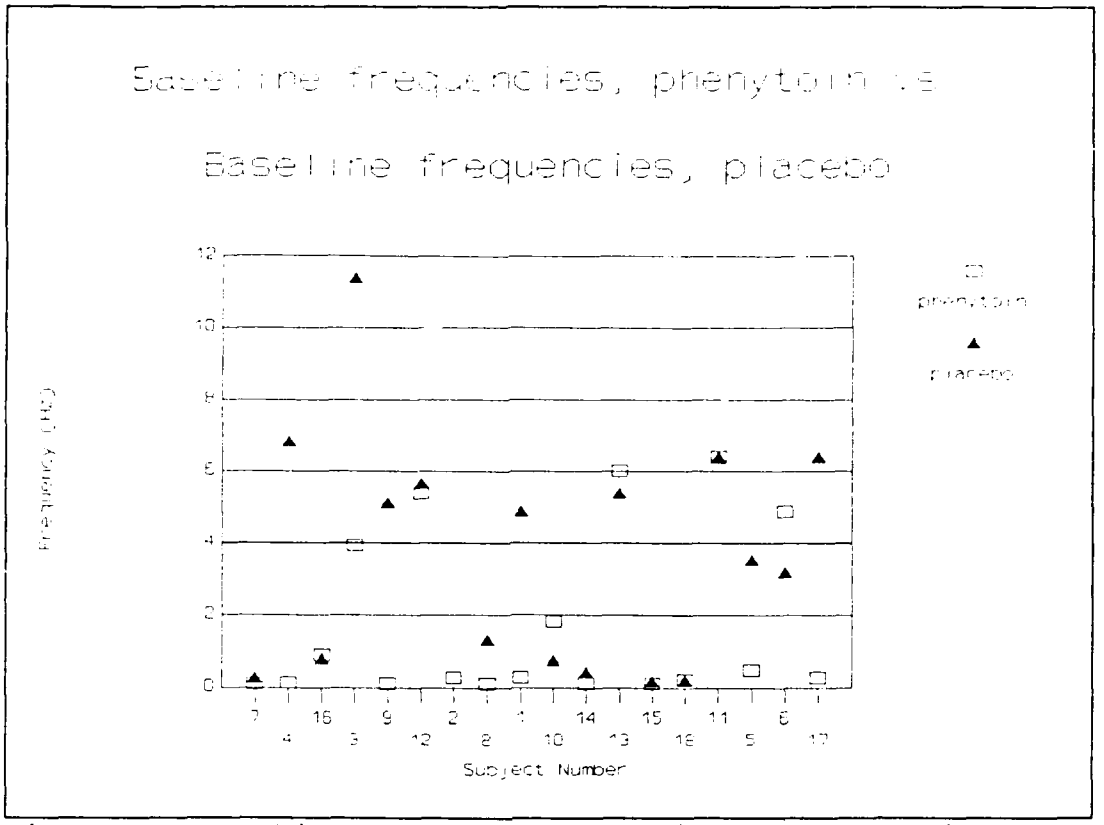

Figure 9. Baseline EEG frequency while on phenytoin versus Baseline EEG frequency while on placebo

Figure 9 graphically represents Table VI. Baseline EEG frequency the baseline-period EEG frequency during each subject's phenytoin or placebo trial. Abscissa is indexed by subject number, according to increasing phenytoin serum levels. Subject 2 had no placebo data recorded.

6. Number of symptomatic periods per phenytoin trial with subdelta EEG frequencies (NUMP) versus the Number of symptomatic periods per placebo trial with subdelta EEG frequencies (NUMPL):

The NUMP compared with the NUMPL (Table VII) is depicted in Figure 10. A general trend seems to be that more subjects have more periods with subdelta frequencies while on placebo than while on phenytoin. Comparing the numbers in Table VII confirms this. Seventy-two percent of the subjects (13 of 18) have more malaise periods with subdelta frequencies while on placebo than while on phenytoin. Only 22% (4 of 18) showed more periods while on phenytoin. Subject 9 recorded the same number of periods for both trials. The paired-t test calculated a p-value of .0019. At a significance level of .05, this suggests that phenytoin may have an impact on the number of malaise periods where peak-amplitude EEG frequencies are in the subdelta range.

Table VII. Number of periods with subdelta frequencies, phenytoin and Number of periods with subdelta frequencies, placebo

Number of periods with subdelta frequencies while on phenytoin vs. Number of periods with subdelta frequencies while on placebo

subject number	number periods phenytoin	number periods placebo
1	0	4
2	1	3
3	2	3
4	1	0
5	0	3
6	0	1
7	2	5
8	0	3
9	4	4
10	1	3
11	3	2
12	3	2
13	4	2
14	0	4
15	1	3
16	1	2
17	0	2
18	1	4
mean number:	1.3	2.78

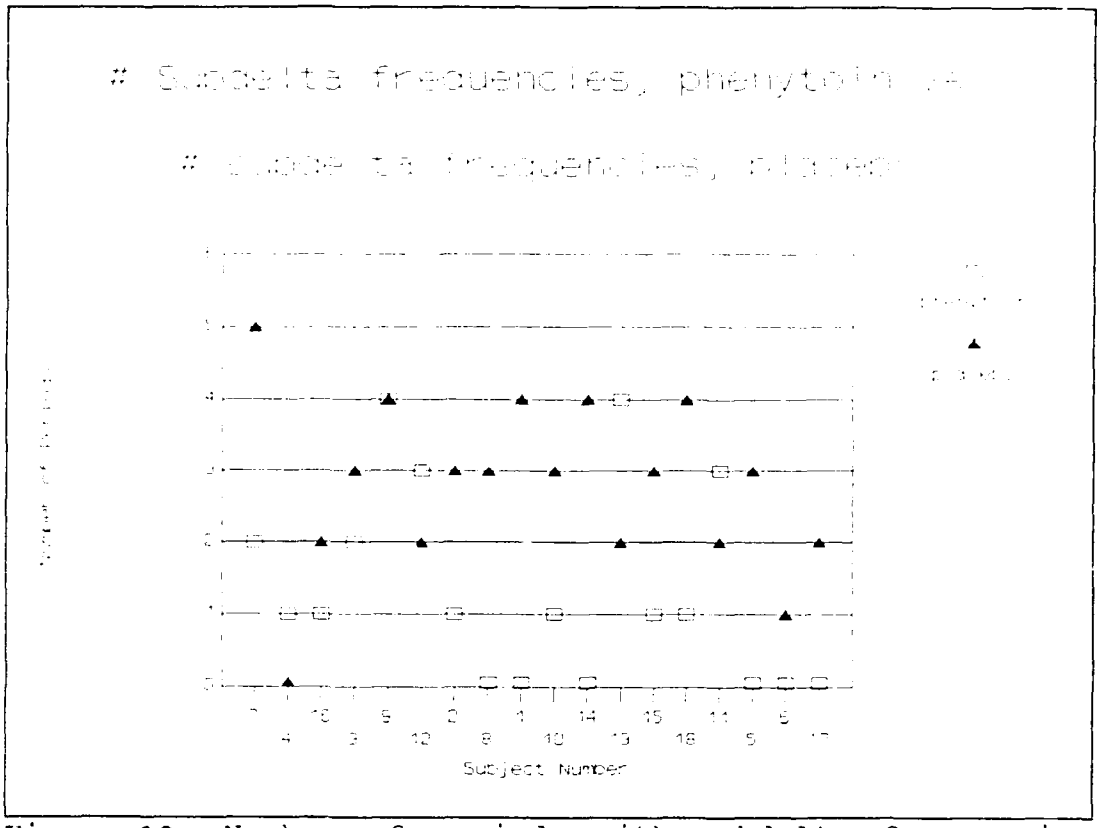

Figure 10. Number of periods with subdelta frequencies while on phenytoin versus Number of periods with subdelta frequencies while on placebo

Figure 10 graphically represents Table VII. Number of subdelta frequencies is the number of periods during each subject's phenytoin or placebo trial that they had a subdelta EEG frequency as the peak-amplitude frequency. Abscissa is indexed by subject number, according to increasing phenytoin serum level.

V. CONCLUSIONS AND RECOMMENDATIONS

Conclusions

Table VIII summarizes the regression analysis results. Table IX summarizes the hypothesis testing results. The significance level for all tests was .05. The following reiterates the data set variable names and their symbols:

LEV--Phenytoin serum level
FREQP--Mean symptomatic EEG frequency, phenytoin trial
BLP--Baseline EEG frequency, phenytoin trial
NUMP--Number of malaise periods per trial with peak-amplitude frequency in subdelta range, phenytoin
FREQPL--Mean symptomatic EEG frequency, placebo trial
BLPL--Baseline EEG frequency, placebo trial
NUMPL--Number of malaise periods per trial with peak-amplitude frequency in subdelta range, placebo

Table VIII. Summary of Regression Analysis results

SUMMARY OF REGRESSION ANALYSIS RESULTS

VARIABLES	ONE-TAILED P-VALUE	R-SQUARED VALUE	RESULT
LEV / FREQP	.0836	.1158	ACCEPT H0
LEV / BLP	.2843	.0207	ACCEPT H0
LEV / NUMP	.1197	.0854	ACCEPT H0

The null hypothesis (H0) stated that there is no relationship between phenytoin serum levels and frontal-midline EEG frequencies; the alternate (H1) stated that a relationship does exist.

Table IX. Summary of Hypothesis Test results

SUMMARY OF HYPOTHESIS TEST RESULTS

Variables	One-Tailed P-value	Result
FREQP / FREQPL	.0886	ACCEPT H0
BLP / BLPL	.0231	REJECT H0
NUMP / NUMPL	.0019*	REJECT H0

(* indicates paired-t test. All others Wilcoxon signed rank test.)

These results strongly suggest that phenytoin serum levels do not significantly influence EEG frequencies.

Furthermore, from Table IX, the comparison of NUMP vs. NUMPL elicited a rejection outcome. This, combined with the results from the regression analysis, suggests that phenytoin suppresses the generation of subdelta EEG frequencies, but no relationship exists between phenytoin serum levels and those frequencies.

A recent supposition (22) suggested that subdelta EEG activity is a defense mechanism and that phenytoin may enhance that activity. This research does not support that assertion. Table VII shows the mean number of periods with a peak-amplitude frequency in the subdelta range for phenytoin trials and placebo trials. The mean for the placebo trials is more than twice the mean for phenytoin trials (2.78 vs. 1.33). If a relationship does exist between phenytoin serum levels and

subdelta activity, it appears that phenytoin suppresses subdelta activity.

Recommendations

1. Continue this technique in EEG analysis, but increase sample sizes. The sample size used in this research limited lower-frequency resolution to .1 Hz. Larger sample sizes will facilitate investigation into lower frequency ranges.

2. Extend cepstral analysis to encompass all EEG channels. Correlating the separate channels could ascertain the coincidence of subdelta EEG frequencies throughout the brain.

3. Some subjects reported hearing changes/impairments under the drug. Do audiometer testing to confirm if this is real or subjective. This data would be useful for detailing the existence of side-effects that impair performance.

4. Incorporate the BIO-LOGIC Brain Atlas System into motion sickness analysis. If motion sickness is truly an analog to a partial seizure, the System can be used to localize the origin of the seizure and map its propagation.

APPENDIX A: PEAK AMPLITUDE AND CORRESPONDING FREQUENCY PER PERIOD PER SUBJECT, PHENYTOIN

SUB.	BL	MI	MIIB	MIIA	MIII	FS
	(FREQUENCY, Hz)					
1	15851	11543				
	(.276)	(4.88)				
2	13735	7674				
	(.276)	(.293)				
3	11281	25882	9956	297732		10592
	(3.94)	(.130)	(5.689)	(.183)		(3.94)
4	18250	12618	9987	8025	9673	9023
	(.138)	(4.88)	(5.39)	(.100)	(3.10)	(10.24)
5	8662	8960	9227	8918	14974	10305
	(.488)	(10.24)	(7.877)	(3.53)	(4.88)	(4.88)
6	7725	11381	13883	11664	10458	8010
	(4.88)	(2.133)	(6.4)	(5.390)	(6.4)	(6.4)
7	6606	11001	7492	11013		10003
	(.100)	(.192)	(5.390)	(5.390)		(.656)
8	9397	8686				
	(.115)	(2.133)				
9	9247	27643	8443	21313	7714	8725
	(.105)	(.258)	(1.862)	(.102)	(.208)	(1.30)
10	6789	11774				7912
	(1.830)	(4.88)				(.4)
11	15246	26615	10879	11800	46540	7580
	(6.4)	(.158)	(.164)	(3.30)	(.179)	(3.2)
12	14097	11650	74587	28364		
	(5.390)	(.192)	(.100)	(.497)		
13	7798	71264	26751	70167	19830	4021
	(6.024)	(.136)	(.212)	(.108)	(.121)	(5.390)
14	10451	8947	7154	10907		17603
	(.127)	(1.078)	(2.93)	(4.88)		(5.390)
15	8162	30175	11992	7703		
	(.120)	(.145)	(5.390)	(6.4)		
16	8949	9562	13202	9299	14111	10127
	(.90)	(.103)	(4.88)	(3.94)	(1.83)	(3.30)
17	16667	7286				
	(.276)	(3.94)				
18	8431	6675	7692	8538		9538
	(.224)	(.378)	(2.84)	(4.88)		(.102)

Blanks indicate no symptoms reported for that malaise period.

PEAK AMPLITUDE AND CORRESPONDING FREQUENCY PER PERIOD PER SUBJECT, PLACEBO

SUB.	BL	MI	MIIB	MIIA	MIII	FS
	(FREQUENCY, Hz)					
1	11543	12522	7334	9750	11996	9739
	(4.88)	(.195)	(.226)	(10.24)	(.180)	(.957)
2			12660	8586	9564	9500
			(.957)	(11.38)	(.276)	(.548)
3	8046	9766	9967	35011	9069	10108
	(11.38)	(.120)	(.115)	(.227)	(3.10)	(6.4)
4	9708	10137	14892	9202	13830	7571
	(6.83)	(2.84)	(2.84)	(3.94)	(1.83)	(4.88)
5	13693	9396	38912	17551	9332	17227
	(3.53)	(.241)	(.139)	(.130)	(1.07)	(5.39)
6	8413	13294	8745	14981	9035	7824
	(3.2)	(.366)	(3.94)	(6.4)	(6.4)	(1.83)
7	14182	10083	7122	10579	6011	9900
	(.276)	(.447)	(.200)	(.143)	(.957)	(.957)
8	10686	10957	180979	147050		13128
	(1.31)	(1.74)	(.147)	(.183)		(.211)
9	12427	38916	23331	65481	188937	14835
	(5.12)	(.119)	(.117)	(.123)	(.135)	(4.88)
10	9096	15768	12436	12033	47329	8173
	(.742)	(6.4)	(6.4)	(.135)	(.119)	(.323)
11	10063	12585	10234	11800	25120	8428
	(6.4)	(.214)	(3.30)	(3.3)	(.139)	(5.38)
12	12419	11964	24291	41114		10325
	(5.68)	(6.4)	(.137)	(.195)		(5.68)
13	11440	19261	7588	8507	11507	10225
	(5.39)	(5.39)	(.632)	(.957)	(1.83)	(5.39)
14	11622	11474	7723	9151	8503	7394
	(.416)	(.276)	(.875)	(.416)	(6.4)	(.147)
15	7364	9876	7469	8722	6656	7340
	(.179)	(.263)	(3.94)	(1.55)	(.120)	(.100)
16	8226	9785	8845		9635	6570
	(.794)	(5.69)	(.154)		(5.12)	(.113)
17	12954	8428	13980	45932	22001	11368
	(6.4)	(4.27)	(5.39)	(.374)	(.188)	(3.94)
18	8409	119654	44681	47607		156857
	(.205)	(.141)	(.170)	(.155)		(.155)

Blanks indicate no symptoms reported for that malaise period except for Subject 2, periods BL and MI. An equipment malfunction prevented recording of that part of the experiment.

APPENDIX B: EEG FREQUENCY STATISTICS FOR SUBJECTS ON PHENYTOIN

Subj	Mean	StDev	Min	Max
1	4.88	0.00	4.880	4.880
2	0.29	0.00	0.290	0.290
3	2.49	2.41	0.130	5.689
4	4.74	3.31	0.100	10.240
5	6.30	2.44	3.530	10.240
6	5.35	1.63	2.133	6.400
7	2.91	2.49	0.192	5.390
8	2.13	0.00	2.130	2.130
9	0.75	0.71	0.102	1.862
10	2.64	2.24	0.400	4.880
11	1.40	1.52	0.158	3.300
12	0.26	0.17	0.100	0.497
13	1.19	2.10	0.108	5.390
14	3.57	1.71	1.078	5.390
15	3.98	2.75	0.145	6.400
16	2.81	1.68	0.103	4.880
17	3.94	0.00	3.940	3.940
18	2.05	1.95	0.102	4.880

EEG FREQUENCY STATISTICS FOR SUBJECTS ON PLACEBO

1	2.360	3.95	0.180	10.240
2	3.300	4.68	0.276	11.380
3	2.000	2.48	0.115	6.400
4	3.270	1.05	1.830	4.880
5	1.400	2.03	0.130	5.390
6	3.790	2.42	0.366	6.400
7	0.540	0.35	0.143	0.957
8	0.570	0.68	0.147	1.740
9	1.070	1.90	0.117	4.880
10	2.680	3.04	0.119	6.400
11	1.500	1.48	0.139	3.300
12	3.100	2.95	0.137	6.400
13	2.840	2.12	0.632	5.390
14	1.620	2.40	0.147	6.400
15	1.190	1.48	0.100	3.940
16	2.770	2.64	0.113	5.690
17	2.830	2.14	0.188	5.390
18	0.155	0.01	0.141	0.170

Statistics are for malaise periods only.

APPENDIX C: CEPSTRUM ANALYSIS

> "The cepstrum exists in various forms but all can be considered as a spectrum of a logarithmic (amplitude) spectrum. This means that it can be used for detection of any periodic structure in the spectrum, e.g. from harmonics, sidebands, or the effects of echoes" (23:161).

"**Ceps**trum" comes from inverting the first syllable of the word "**spec**trum". It originated in 1963, and its first intended application was in seismic signal analysis (23:162).

Cepstral analysis was chosen for this research because of its ability to detect periodicity in the spectrum that is not readily apparent to the eye, and its capability to measure that periodicity very accurately (23:184-186).

Using F: to represent the Fourier Transform of the bracketed quantity, the cepstrum if defined as

$$c(t) = |F:\{ \log F_{xx}(f) \}| \qquad (2)$$

where $F_{xx}(f)$ is the power spectrum of the time signal $f_x(t)$ and

$$F_{xx}(f) = |F: \{ f_x(t) \}|^2 \qquad (3)$$

(23:163-164)

A periodic signal gives a periodic structure to the spectrum, which in turn becomes an impulse function in the

cepstrum (23:171). A set of typical signals is shown in Figure 11. Cepstrum ordinate metric is "relative power".

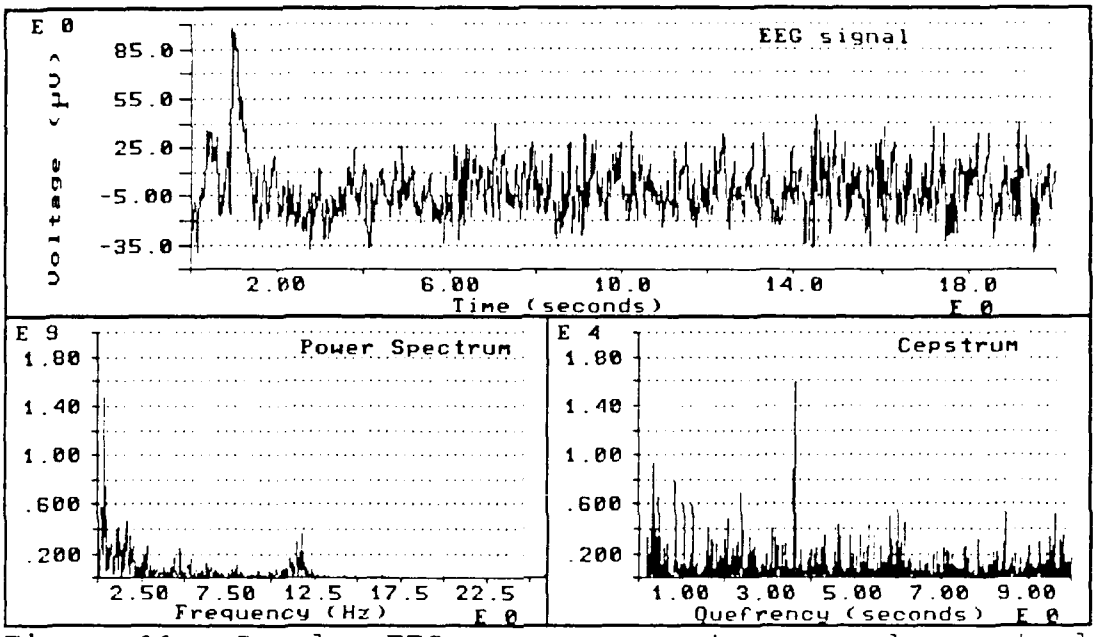

Figure 11. Sample EEG, power spectrum, and cepstral signals

The top signal is EEG data from the frontal-midline area of the skull. Voltage levels are skin-surface values. The corresponding power spectrum is shown in the lower left.

No periodicity is readily evident in the power spectrum, but the cepstrum (lower right) detected some periodicity. The frequency of the periodicity in Hertz is obtained simply by inverting the quefrency value. Quefrency is the X-axis of the cepstrum. "**Quefr**ency" comes from inverting the first syllable of the word "**frequ**ency" (23:171). In this example, that frequency is approximately .27 Hz. Some signal does appear in the power spectrum around .27 Hz, but the cepstrum clearly shows a .27 Hz periodic structure within the power spectrum.

Figure 12 depicts a set of cepstral graphs used in this research. All were derived from EEG signals similar to those shown in Figure 11.

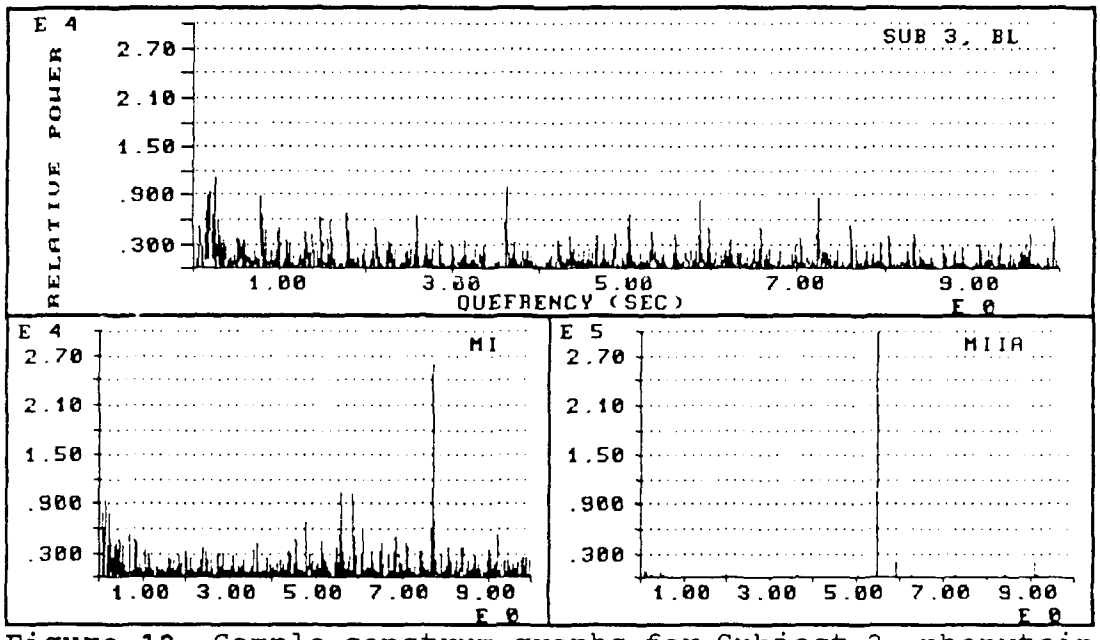

Figure 12. Sample cepstrum graphs for Subject 3, phenytoin trial

Malaise periods are indicated within the graphs. BL is the baseline period (subject in chair, prior to rotation). MI and MIIA are Graybiel malaise periods. MI is defined as slight malaise, or, the initial awareness of any sickness indicator. MIIA is moderate-to-severe malaise, identified by the presence of two or more sickness indicators (20). Note the scale change of the ordinate for period MIIA.

Figure 12 also demonstrates how a cepstrum shows the relative contribution of component signals to the original signal. In malaise period MIIA, the signal producing the .182 Hz (5.5 seconds on the quefrency scale) constitutes almost 30

percent of the total power of the original signal. Conversely, for the baseline period (BL), no one signal dominates the structure.

BIBLIOGRAPHY

1. Chelen, Dr. William and others. "Evaluation of the Therapeutic Efficacy of Dilantin and the Combination Dilantin/Dextromethorphan in the Prevention of Motion Sickness During Weightless/Parabolic Flight," Air Force Institute of Technology, AFIT/ENG Research Protocol, 29 Dec 1988.

2. Chelen, Dr. William. Research Contractor, AFIT/ENG. Personal Interview. AFIT/EN, Wright-Patterson AFB OH, June 1988-April 1989.

3. Chelen, Dr. William and others. "Electroencephalographic Changes During Motion Sickness." Pre-publication copy. Air Force Institute of Technology/ENG, 1987.

4. Cowings, Patricia S., Ph.D. "Autogenic-Feedback Training: A Treatment for Motion and Space Sickness." Pre-publication copy, sent to CRC Press for inclusion in the book Motion and Space Sickness (ed. by George Crampton) 1988.

5. Davis, Dr. Jeffrey R. and others. "Space Motion Sickness During 24 Flights of the Space Shuttle," Aviation, Space, and Environmental Medicine,59: 1185-1189 (December, 1988).

6. Dhenin, Geoffrey. Aviation Medicine: Physiology and Human Factors. London: Tri-Med Books Limited, 1978.

7. Drylie, Capt. Michael E. An Analysis of Physiological Data Related to Motion Sickness for Use in a Real-time Motion Sickness Indicator. MS thesis, AFIT/GE/ENG/87D-16. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1987 (AD-189589).

8. Earl, Capt. Orville A. and Charles N. Peterson. Physiological Data Acquisition System and Motion Sickness Prevention Trainer. MS thesis, AFIT/GE/EE/ENG/83D-19. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1983 (AD-138361).

9. Fitzpatrick, Capt. Douglas G., Capt. Michael A. Rogers, and Capt. Robert Williams. Computerized Biophysical Data Acquisition System for Motion Sickness Studies. MS Thesis, AFIT/GE/GCS/ENG/84D-30. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1984 (AD-151691).

10. Fix, Capt. Edward L. Motion Sickness: Quantitative, Algorithmic Malaise Indication in Real Time. MS Thesis, AFIT/GE/ENG/87D-18. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1987 (AD-A189674).

11. Gaudreault, Capt. Pierre J. Motion Sickness: A Study of Its Effects on Human Physiology. MS Thesis, AFIT/GE/ENG/87D-20. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1987 (AD-188821).

12. Graybiel, Ashton, M.D., and James R. Lackner, Ph.D. "Treatment of Severe Motion Sickness with Antimotion Sickness Drug Injections," Aviation, Space, and Environmental Medicine: 773-776 (August 1987).

13. Harm, Deborah L. "Physiology of Motion Sickness Symptoms and Methodological Considerations," NASA report, NASA Johnson Space Center, Houston, Texas.

14. Hartle, Capt. Dana R. A Motion Sickness Prediction Model and System Description. MS thesis, AFIT/GCS/ENG/86D-3. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1986 (AD-177716).

15. Isaksson, Anders and others. "Computer Analysis of EEG Signals with Parametric Models," Proceedings of the IEEE, vol. 69, no. 4. 451-460. New York: IEEE Press, April 1981.

16. Jarvis, Capt. Norman R., and Capt. Charles T. Uyeda. An Analysis of Potential Predictive Parameters of Motion Sickness Using a Computerized Biophysical Data Acquisition System. MS thesis, AFIT/GSO/ENG/85D-1. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1985 (AD-164099).

17. Kabrisky, Dr. Matthew. Professor of Electrical Engineering, AFIT/ENG. Personal Interview. AFIT/EN, Wright-Patterson AFB OH, June 1988-April 1989.

18. McPherson, Capt. Michael R. A Collection and Statistical Analysis of Biophysical Data to Predict Motion Sickness Incidence. MS Thesis, AFIT/GCS/ENG/86D-21. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1986 (AD-178874).

19. Miller, Capt. Robert D. Motion Sickness: A Study of Its Etiology and Statistical Analysis. MS thesis, AFIT/GCS/ENG-/86D-2. School of Engineering, Air Force Institute of

Technology (AU), Wright-Patterson AFB OH, December 1986 (AD-A177786).

20. Miller, Earl F., Ph.D., and A. Graybiel. "A Provocative Test for Grading Susceptibility to Motion Sickness Yielding a Single Numerical Score." Acta Otolaryngologica, Supplement 274, Naval Aerospace Medical Institute, Pensacola, Fla., 1970.

21. Montgomery, Gerald J. and others. Diagnostic Abductive and Inductive Reasoning. Volume I of Phase I Final Report submitted to Flight Dynamics Laboratory, Air Force Wright Aeronautical Laboratories, Wright-Patterson AFB, under contract number F33615-87-C-3610 by Barron Associates, Inc. January 1988.

22. Morales, Capt. Rogelio, Jr. A New Perspective in the Etiology, Treatment, Prevention, and Prediction of Space Motion Sickness. MS Thesis, AFIT/GSO/ENG/88D-2. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1988 (AD-A205660).

23. Randall, R. B., and Jens Hee. "Cepstrum Analysis, " Digital Signal Analysis: Using Digital Filters and FFT Techniques. Selected Reprints from Technical Review. Dayton, OH: Bruel & Kjaer Instruments, Inc., August 1981.

24. Scott, Capt. Mark F. A Study of Motion Sickness: Mathematical Modeling and Data Analysis. MS Thesis, AFIT/GEO/ENG/88D-4. School of Engineering, Air Force Institute of Technology (AU), Wright-Patterson AFB OH, December 1988 (AD-A202770).

25. Thornton, William E. "Clinical Characterization and Etiology of Space Motion Sickness," Aviation, Space, and Environmental Medicine: A1-A8 (September 1987).

Vita

Captain Russel B. Smith [redacted] He graduated from Glendale Junior-Senior High School in May of 1975 and subsequently enlisted in the Air Force. His first assignment was to Howard Air Force Base, Panama Canal Zone, Republic of Panama. He was then assigned to Whiteman Air Force Base in Knob Noster, Missouri. In 1978 he was chosen to attend the Air Force Academy Preparatory School in Colorado Springs, Colorado. In 1979 he entered the Air Force Academy, graduating in 1983 with a Bachelor of Science degree in Biology. Following training at Lowry Air Force Base in Denver, Colorado, he was assigned to Air Force Space Command in Colorado Springs, Colorado, and worked in the Space Surveillance Center and Space Defense Analysis Center in Cheyenne Mountain Air Force Station. After working in Cheyenne Mountain, he was transferred to the 1013th Combat Crew Training Squadron at Peterson Air Force Base, Colorado Springs, Colorado. In May of 1988, he was assigned to the Air Force Institute of Technology at Wright-Patterson Air Force Base.

[redacted]

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved
OMB No 0704-0188

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT APPROVED FOR PUBLIC RELEASE; DISTRIBUTION UNLIMITED
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) AFIT/GSO/ENG/89D-1	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION SCHOOL OF ENGINEERING 6b. OFFICE SYMBOL (If applicable) AFIT/ENG	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) AIR FORCE INSTITUTE OF TECHNOLOGY WRIGHT-PATTERSON AFB, OH 45433	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION ARMSTRONG MEDICAL RESEARCH LABORATORY 8b. OFFICE SYMBOL (If applicable) AAMRL/CC	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code) ARMSTRONG MEDICAL RESEARCH LABORATORY WRIGHT-PATTERSON AFB, OH 45433	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. / PROJECT NO. / TASK NO / WORK UNIT ACCESSION NO

11. TITLE (Include Security Classification)

A Cepstral Analysis of EEG Signals in Motion Sickness Studies (UNCLASSIFIED)

12. PERSONAL AUTHOR(S)
Russel B. Smith, B.S., Captain, USAF

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
MS THESIS	FROM _____ TO _____	1989 DECEMBER	80

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	Motion sickness, space motion sickness, cepstrum, phenytoin, Dilantin, electroencephalogram
06	10		
20	03		

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

THESIS CHAIRMAN: Matthew Kabrisky, PhD.
Professor of Electrical Engineering
Department of Electrical Engineering

ABSTRACT ON BACK

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	
22a. NAME OF RESPONSIBLE INDIVIDUAL Matthew Kabrisky, PhD. Professor of Elec. Eng	22b. TELEPHONE (Include Area Code) (513) 255-5276 / 22c. OFFICE SYMBOL AFIT/ENG

DD Form 1473, JUN 86 Previous editions are obsolete SECURITY CLASSIFICATION OF THIS PAGE

Block 19. Abstract

Eighteen male subjects were given the drug phenytoin in a double-blind placebo-controlled crossover experiment. Subjects were rotated in a motion chair while eight physiological parameters were measured.

This research analyzed frontal-midline EEG signals for trends. Cepstral transformations were used to isolate peak-amplitude EEG frequencies during the evolution of motion sickness. Regression analysis and paired-t tests were applied to this data to identify relationships between phenytoin serum levels and EEG frequencies. Although the drug delayed or prevented the onset of emesis, no statistically significant relationships were found between phenytoin serum levels and frontal-midline EEG signals.